REMARKS/ARGUMENTS

With this amendment, claims 1-28 are pending. Claims 2-8 are withdrawn. Claims 9, 16, 23-25 and 29 are cancelled without prejudice. For convenience, the Examiner's rejections are addressed in the order presented in a March 6, 2007, Office Action.

I. Status of the claims

Claim 10 is amended to correct an error in dependency and to recite full length human ADNF III polypeptide. Support for this amendment is found throughout the specification, for example at paragraph 19. Claims 15 and 22 are amended to correct alleged grammatical errors. These amendments add no new matter.

Rejections Maintained

II. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claims 1, 10-15, 17-23, and 26-28 are rejected under 35 U.S.C. §112 first paragraph, because the specification allegedly does not enable treatment of multiple sclerosis (MS) using the recited genus of ADNF III peptides. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection. The Office Action also alleges that the specification does not enable prevention of MS using the claimed methods. In order to expedite prosecution, claim 1 is now amended to recite treatment of multiple sclerosis. In addition, claim 10 is now amended to recite full length human ADNF III.

The Office Action alleges that undue experimentation is required to practice the claimed methods because identification of active ADNF III peptides is allegedly unpredictable and would require undue experimentation on the part of one of skill in the art. Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention (*see*, *Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988)). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides

a reasonable amount of guidance with respect to the direction in which the experimentation should proceed" (*see*, *Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982)).

Applicants provide a declaration from Dr. Illana Gozes and supporting evidence to demonstrate that the claimed methods are enabled. First, the Office Action cited references, as supporting the rejection for alleged lack of enablement, *e.g.*, Tischer *et al.* (US Patent 5,194,596); Kopchick (US Patent 5,350,836); Skolnick *et al.* TIBS 18:34-39 (2000) and Smith *et al.*, (Nature Biotechnology 15:1222-1223 (1997). Dr. Gozes reviewed the references and disagrees with the analysis of the Office Action. According to Dr. Gozes, the Skolnick and Smith references do not apply to ADNF III peptides because their function has been experimentally determined. The other cited references, Tischer *et al.* and Kopchick support the usefulness of sequence alignments for identifying amino acid residues that, if mutated, are most likely to affect protein activity. Kopchick also demonstrate that results of amino acid substitutions can be predicted by those of skill. Thus, the references cited by the Office Action do not support a rejection for alleged lack of enablement.

Dr. Gozes also discusses the art accepted model that is available to those of skill to identify active ADNF III peptides. According to Dr. Gozes, myelin-oligodendrocyte glycoprotein (MOG)-induced chronic experimental autoimmune encephalomyelitis (EAE) model is an art accepted model of multiple sclerosis. The specification at paragraphs 101-107 provides demonstration of use of MOG-induced EAE to assess the anti-MS activity of ADNF III peptides. According to Dr. Gozes undue experimentation is not required to identify active ADNF III peptides using the MOG-induced EAE model system.

The Office Action also alleges that identification of functional ADNF III polypeptides is unpredictable because of use of a peptide comprising the ADNF III core sequence as an inactive control in the PCT publication WO/20002785. Dr. Gozes states that the inactive control peptides was identified in routine experiments performed to determine the core active site of the full length ADNF III peptide. Also according to Dr. Gozes, similar experiments can be performed using the MOG-induced EAE model system. Thus, the inactive control

peptide of PCT publication WO/20002785 does not support arguments against the enablement of the claimed methods.

The Office Action also alleges that there is no evidence that an all D-amino acid ADNF III core peptide would have a biological function. Dr. Gozes points out that the all D-amino acid ADNF III core peptide was known to have neuroprotective activity at the time of filing. Dr. Gozes also provides evidence that the related all D-amino acid ADNF I core peptide has activity in the MOG-induced EAE model system. As the ADNF I and ADNF III peptides have similar activities in many systems, Dr. Gozes states her belief that an all D-amino acid ADNF III core peptide would function similarly to all D-amino acid SAL in the MOG-induced EAE model system.

In order to establish a prima facie case of lack of enablement, the Examiner has the burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The Examiner has not provided any reason why those of skill would not be able to use the genus of ADNF III peptides to treat MS. Applicants, therefore, respectfully assert that based on the disclosure of the specification and the state of the art at the time of filing, the claimed methods are enabled.

In view of the above amendments and arguments, withdrawal of the rejection for alleged lack of written description is respectfully requested.

III. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 1, 10-24, and 26-28 are rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. According to the Office Action, the specification does not provide adequate description of the genus of ADNF III polypeptides that comprise SEQ ID NO:2. The Office Action alleges that those of skill would not recognize that the inventors had possession of the claimed invention at the time of filing and objects specifically to the description of full length ADNF III polypeptides. In response, Applicants respectfully traverse the rejection.

As US patent law is currently applied, the specification does describe the distinguishing characteristics of a genus of ADNF III amino acid sequences. The Federal Circuit

court of Appeals addressed the description adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. *See, e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). An applicant may also show that an invention is complete by

> . . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Id.* at 1613.

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *See, e.g.*, 66 Fed. Reg. 1099, 1106 (2001).

Here the specification provides the structure of the ADNF III core sequence, *i.e.*, SEQ ID NO:2, and the correlating function, *i.e.*, treatment of multiple sclerosis. The specification also provides an art accepted model to assess the ability of an ADNF III peptide to provide treatment of MS. The claimed genus is the group of polypeptides that comprise SEQ ID NO:2 and have the disclosed function. Functional assays and experimental data from an art accepted model are disclosed in the specification, *e.g.*, at page 22, line 4 through page 24, line 10 and at page 30, line 1 through page 31, line 11. As the specification discloses the polypeptide structure and experimental data to support the claimed function, those of skill would understand that the inventors had possession of the claimed invention at the time of filing.

The Office Action again cites known ADNF III sequences and alleges that such sequences must be recited in the specification or sequence listing to provide description of the claimed genus. This position is inconsistent with recent decisions by the Federal Circuit Court of Appeals. First, the Federal Circuit has made it clear that there is no per se rule regarding inclusion of sequence information in a patent application to support description of a nucleic acid sequence, and by analogy an amino acid sequence. "When the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh."

Capon v. Eshar, 76 USPQ2d 1078, 1084-5 (Fed. Cir. 2005). In fact, the Federal Circuit has recently ruled that even incorporation by reference of known sequences is not required for the written description requirement. "Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences. . . , satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted)of such genes and sequences." *Falkner v. Inglis*, 79 USPQ2d 1001, 1008 (Fed. Cir. 2006). Thus, the genus of ADNF III polypeptides used in the claimed methods is adequately described. More disclosure is not required to demonstrate that the inventor's had possession of the genus at the time of filing.

In view of the above amendments and arguments, withdrawal of the rejection for alleged lack of written description is respectfully requested.

New Claim Rejections

IV. Rejections under 35 U.S.C. §112, first paragraph, enablement

Claim 1 and dependent claims 24, 16, and 29 are rejected as allegedly being directed to non-enabled subject matter. In order to expedite prosecution, claims 24, 16, and 29 are cancelled. Withdrawal of this rejection for alleged lack of enablement is respectfully requested.

V. Rejections under 35 U.S.C. §112, first paragraph, written description

Claim 1 and 29 are rejected as allegedly failing to comply with the written description requirement. In order to expedite prosecution, claim 29 is cancelled. Withdrawal of this rejection for alleged lack of written description is respectfully requested.

VI Rejections under 35 U.S.C. §112, second paragraph

Claim 10 is rejected as allegedly indefinite for depending from a cancelled claim. In order to expedite prosecution, claim 10 is amended to depend from claim 1. Claims 1, 23, and 24 are rejected as allegedly indefinite and confusing. In order to expedite prosecution, claims 23

and 24 are cancelled. In view of these amendments, withdrawal of the rejection for alleged indefiniteness is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

/Beth L. Kelly/

Beth L. Kelly
Reg. No. 51,868

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
BLK:blk
61068904 v1